UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

FEDERAL TRADE COMMISSION, Plaintiff, v. DIRECT MARKETING CONCEPTS, INC., et al, Defendants	CIVIL ACTION NO. 04-CV 11136GAO

DECLARATION OF RONALD J. AMEN, PH.D.,
IN RESPONSE TO THE DECLARATION OF MARY LEE VANCE, M.D.
REGARDING HER REVIEW OF RENUVA™ AND ITS INGREDIENTS

I, Ronald J. Amen, hereby declare as follows:

Introduction and Qualification

1. My education consists of a Bachelors degree in Biology from Bethany College, Bethany, West Virginia, a Master of Science degree in Food Science from Rutgers University, New Brunswick, New Jersey, and a Doctor of Philosophy degree from Rutgers. My doctoral concentration and thesis was in the field of nutritional physiology, in the Department of Food Science. I have also taken graduate level classes in molecular biology (SUNY), physiology (Long Island University) and business (Santa Clara University).
2. I am presently the President of Techenterprises, LLC, a consulting company whose clients primarily consist of start-up or emerging pharmaceutical and/or nutrition companies seeking regulatory, clinical, and product development advice. I am currently a member of the Board of Directors of three of these emerging pharmaceutical companies, one nutrition company, one metrology company, and one start-up hydroscience company.
3. For 15 years I was a Partner in the consulting firm of ABIC International Consultants, Inc. ABIC's clients included many of the world's largest domestic

and international-based food, nutrition, and pharmaceutical companies. I was primarily responsible for the product development and clinical research activities of ABIC's pharmaceutical and nutrition clients.

4. I have also held executive positions in several companies. I was President of Nextech Healthcare, Inc. for five years. This company developed and marketed nutritional products and laboratory test kits. I was interim President of Avicena Group, Inc, an emerging pharmaceutical company. Prior to these endeavors, I was Director of Clinical Research and Product Development for American McGaw Laboratories, Inc. McGaw's product line consisted of a full range of intravenous drugs and clinical nutrition products. Before working at McGaw, I was Head of Nutritional Sciences for Syntex Research Corporation, Inc. Syntex developed and marketed enteral clinical nutrition and infant formula products.
5. I am presently the Chairman of the Food Science Industry Advisory Committee to Chapman University (Orange, CA), and have served on the University's Science Advisory Board. Occasionally, I have taught graduate-level courses at Chapman, and remain an Adjunct Professor. I have also served on the Science Advisory Board of Saddleback College (Mission Viejo, CA).
6. Despite being restricted by corporate confidentiality, I have published a number of nutritional and pharmaceutical science papers in peer-reviewed journals, and co-edited two books on dietary fiber. Additionally, I have previously been granted several patents in the nutrition and pharmaceutical fields.
7. An accurate and current curriculum vitae is provided as an addendum to this Declaration.

Background and Discussion Regarding the Mechanism of Action of the Renuva™ System

1. The Renuva System, produced by Anti-Aging Formulas, Inc. (AAF) consists of a spray called the "Infuser," and a reconstitutable powder called the "Generator." AAF contends that the administration of the components of this dual system will activate and up-regulate the secretion of Growth Hormone (GH). This enhanced secretion of GH should then, in turn, lead to increased levels of Insulin-like

Growth Factor-1 (IGF-1), which is the hormone that is credited with imparting the benefits seen after GH secretion or administration.

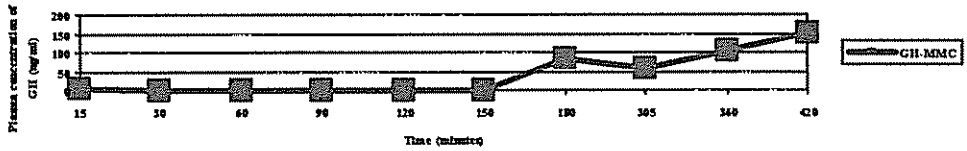
2. It is indisputable that as one ages GH levels of the body decrease, and as a result, certain physiological effects occur. Among these effects are decreased energy and stamina, decreased lean body mass, compromised skin texture and appearance, an erosion of cognitive powers and memory, and other effects mentioned in the infomercial.

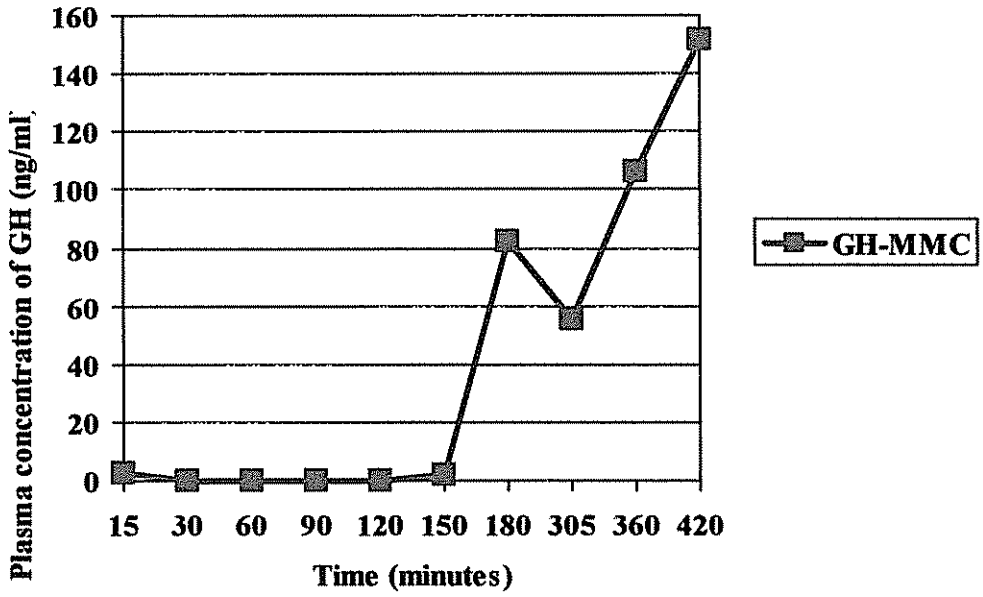
3. The scientific community also believes that increased levels of GH, and subsequent increases in IGF-1, will, in a substantial number of individuals, reverse many of these undesirable physiological effects that we attribute to normal aging. The reversing of these effects is collectively termed "anti-aging." The aging characteristics that have been shown to be reversed by the supplementation of GH include, but are not limited to, those presented in the infomercial; among which are increased energy and stamina, increased lean body mass, improved skin texture and appearance, and improved memory and cognition.

4. The primary issue to be discussed, therefore, is whether the Company's claims that the Renuva system can influence these characteristics of aging, if not in fact, then at least in theory, can be substantiated. To be examined are the questions of whether there is any evidence that the ingredients of the Infuser and Generator formulas are capable of remaining intact until they reach the blood-brain barrier (i.e. not hydrolyzed by gastrointestinal acids or enzymes, or not catabolized by enzymes in the liver); whether there is any evidence that the ingredients are able to penetrate the blood-brain barrier and reach the pituitary gland; and whether there is any evidence that the ingredients are efficacious in up-regulating and releasing the secretion of GH.

5. The Infuser contains an array of peptides that have been enveloped in a proprietary delivery-system polymer patented by the University of Illinois, and licensed to the supplier of AAF's peptide component. The system, known as Advanced Macro-Molecular Complex (MMC-2000) is designed to orally deliver large molecular weight proteins (e.g. Insulin or Growth Hormone). The graph

below shows that the MMC system is capable of delivering GH to the plasma without degradation. Thus, there does not appear to be any reason to suspect that MMC will not be able to deliver un-degraded GHRP to the plasma.





6. It is well established that a peptide produced in the hypothalmus, known as the Growth Hormone-Releasing Hormone (GHRH), is primarily responsible for the secretion of GH. Other peptides, known as Growth Hormone-Releasing Peptides (GHRP) are also capable of causing this secretion. Thus, it could be argued, that if peptides with hormone-releasing activity could cross the blood-brain barrier intact, they could link with the receptor sites on the anterior portion of the pituitary (G protein-coupled transmembrane receptors), and effect an enhanced secretion of GH.

7. It is known that, due to the presence of acid and enzymes, peptides are difficult to ingest, digest, and be absorbed through the intestinal mucosal wall in an unaltered state. Additionally, those that are absorbed intact may be transported directly to the liver where they will be exposed to catabolic enzymes. To insure that enough "active" peptides reach the blood-brain barrier intact, it would be necessary to by-pass both the gastrointestinal tract and the liver ("first pass effect"). By introducing the peptide components directly to the blood stream by mucosal absorption in the mouth, the peptide mixture is absorbed into the body without exposure to the gastrointestinal tract or the liver. This direct absorption of peptides into the venous system is similar to the effect one sees when one injects a compound subcutaneously.
8. Once in the blood stream, peptides of the amino acid residue number under discussion are difficult to pass through the blood brain barrier. However, the proprietary delivery system developed by the University of Illinois is capable of transporting the peptides across the blood-brain barrier. The University of Illinois data indicate that the peptide-hormone, GH, can be transported across the blood-brain, and that the peptide transportation occurs in a time-release manner, thus sustaining the effect of the peptide in the brain.
9. The Renuva Infuser contains, among other components, peptides that are known to have GHRP activity. Thus, if the peptides can be absorbed and delivered to the blood-brain barrier intact, and then transported across the blood-brain barrier, it is reasonable to conclude that some of the peptides may activate the receptor sites residing in the anterior portion of pituitary, and instigate a secretion of GH.
10. The administration of enteral GHRH and GHRP analogues to increase GH production and secretion has recently been demonstrated. Butter et al[1] administered a trans-dermal GHRH analogue-peptide to 35 active and sedentary men and women. They reported: "Within the first week, changes experienced were overwhelmingly positive. Improvements were reported of 282.98% in the female subjects and 352.38% in male subjects. Muscle strength increased by 81.0%. Endurance increased by 60.0%. Quality of sleep improved by 92.6%.

Overall energy increased by 71.4%. Total mean improvement of all 4 objective criteria increased by 76.6%. See table below.

	Sum Totals for All Objective Criteria						
	12 H	24 H	36 H	48 H	60 H	72 H	84 H
Strength	4	11	15	16	20	24	21
Energy	10	12	19	19	21	19	25
Endurance	2	11	18	19	22	26	27
Sleep	6	15	17	19	19	21	21
Totals	22	49	69	73	82	90	94

11. A 2005 study[2] reported that the administration of an oral growth hormone secretagogue (i.e. GHRP) was able to induce a significant rise in GH levels. The open, randomized, placebo-controlled dose-escalation study involved a total of 36 healthy male volunteers, divided into groups so that three different doses of the peptides and/or a placebo were received. All subjects had been initially checked for their ability to release GH by the intravenous administration GHRH. The data demonstrated that between 1-2 hours after GHRP administration there was a statistically significant increase in the levels of GH in the blood without any effect on other hormones with the mean GH value being 79.12 ng/ml at the highest dose of GHRP ($p=0.009$), compared to 52.62 ng/ml with GHRH and 3.58 ng/ml for placebo. In all cases the peptide was well tolerated and no adverse events were reported.

12. AAF reports that the ingredients in the Renuva™ Generator include amino acids, vitamins, minerals, and other common nutritional components present in many dietary supplement products. These ingredients were chosen by the Company because there have been publications linking some of these ingredients to increased secretion of GH, and other ingredients to the alleviation or reduction in some of the physiological manifestations of aging, including loss of memory, loss of energy, and decreased joint health.

13. The Renuva™ Generator contains amino acids that have also been identified in peer-reviewed scientific journals as biochemicals that up-regulate GH secretion

(secretagogues). Among the secretagogues contained in the Renuva™ Generator are arginine, glutamine, glycine, lysine, ornithine, and glutamic acid. These secretagogues activate receptor sites on the posterior portion of the pituitary, and thus work in concert with, and in support of, the secretagogue effect of the Renuva™ Infuser.

14. L-Tyrosine is another component of the Generator. This amino acid is a precursor for as much as 90% of the production of the neurotransmitters, such as dopamine, and epinephrine. Scientists believe that one of the main causes of stress-related depression or mental fatigue is directly related to decreased levels of dopamine, and other neurotransmitters in the brain. L-Tyrosine is believed to up-regulate the production of neurotransmitters and maintain their levels when the body is under duress.

15. Gamma Amino Butyric Acid (GABA) is an amino acid derivative that functions as an inhibitory neurotransmitter of the central nervous system. It is an anti-stress, anti-anxiety, calming and relaxing nutrient. It has been used clinically for depressed sex drive, prostate problems, and as a non-addictive tranquilizer substitute, and helps induce relation and sleep. Additionally, GABA has been shown to activate the anterior pituitary to release GH.

16. Finally, the Generator contains niacin and Vitamin C. Niacin is not only a required B vitamin, but is also an up-regulator of GH. Vitamin C is both a powerful anti-oxidant and a necessary biochemical for structural tissue integrity.

Review of the Declaration of Dr. Mary Lee Vance

1. Dr. Vance has focused her criticisms of the Renuva™ system on the Company's reliance on published data generated from studies in which GH was injected into subjects. She argues "The studies discussed above were conducted using injected (subcutaneous, under the skin) GH. Studies of the effect of GH administration use injected (subcutaneous) GH because growth hormone is broken down (degraded) by gastric acid, and thus oral GH would not be expected to be effective."

2. Her summary position, as stated above, suggests that she has missed two very important, and pivotal points, as they relate to the formulation and delivery of the

Renuva™ Infuser system. First, Renuva is not delivering GH, but rather GHRP. Second, and critically, the GHRP are absorbed through the mucosa in the mouth. This prevents the degradation of the GHRP by gastric acid since the GHRP are never introduced to the stomach, and are never exposed to gastric acid. Since the GHRP are then transported directly into the blood stream, the end result is the same as if the GHRP had been injected. The GHRP are carried by the blood to the blood-brain barrier, and are transported across the blood-brain barrier by the patented (and proven) sustained-release transport system technology from the University of Illinois.

3. Based on the positions that (a) the GHRP enter the blood stream in an unaltered fashion (similar to if they had been injected), (b) that the GHRP cross the blood-brain barrier (as demonstrated by the University of Illinois and others), (c) that it is known, and has been demonstrated, that GHRP causes the secretion of GH from the pituitary, and (d) that GH, perhaps through its up-regulation of IGF-1, causes demonstrable changes in physiology, it is AAF's belief that the data obtained from subjects that received subcutaneous injections of GH are directly transferable to the effects that would be seen after administration of the Renuva Infuser system. Additionally, Renuva™ system contain other GH up-regulating biochemicals working in concert with the GHRP,

As a result of my understanding of the purported effects of the ingredients in the Renuva™ system, and the effects of GH and IGF-1 on the body's physiology, I believe that it is reasonable for AAF to have concluded that the effects seen after injections of GH could be reasonably attributed to those that would be seen after administration of the Renuva™ system. The information presented in the infomercial appears to reasonably support their hypothesis.

I hereby declare under penalty of perjury that the foregoing is true and correct to the best of my knowledge.

Signed: Ronald J. Amen, Ph.D. Date: June 7, 2005

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[1] Butter RA, DC Viktora, ME Quinn. Accelerated And Efficacious Results Using Variable Somatotroph And Hypothalamotroph Specific Poly-Peptide Combinants Utilizing A Trans-Dermal Delivery Mechanism (Td-Ghrh-A) As An Alternative To Recombinant Human Growth Hormone Injection Therapy J Integrative Medicine 2000;4:51-61.

[2] AEterna Zentaris Announces Phase I Positive Results for its Oral Growth Hormone Secretagogue Compound EP-1572. Yahoo Finance. 2005.